of the adherent molecules on erythroblasts. Further studies are needed to clarify this point.

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Leukoerythroblastosis Following the Use of G-CSF

To the Editor: We read with great interest the letter presenting a case of pseudoleukemia following the use of granulocyte colony-stimulating factor (G-CSF) by Reykdal et al. in the July 1995, issue of the *American Journal of Hematology* [1]. Increase in the count of both mature and immature forms of neutrophils with certain changes in morphology is the expected impact of G-CSF on the peripheral blood. Although early precursors of the myeloid lineage such as myelocytes, promyelocytes, and even blasts have been readily observed on peripheral blood smears after G-CSF treatment, a full-blown picture of leukoerythroblastosis has not so far been reported [1,2].

We present here a patient with acute myelomonocytic leukemia (AML-M4) who has exhibited a leukoerythroblastic blood picture after the administration of G-CSF. A 48-year-old male patient was admitted to the hospital with gingival hypertrophy and constitutional symptoms of abrupt onset. Laboratory work-up revealed a white blood cell count of 96.8×10^9/L, erythrocyte sedimentation rate of 78 mm/hr and serum lactate dehydrogenase level of 1,581 U/L; the remaining biochemical parameters were within normal limits. Peripheral smear yielded a differential count of 84% blasts, 2% promyelocytes, 2% metamyelocytes, 5% bands, 2% polymorphonuclear leukocytes, and 5% lymphocytes with normal erythrocyte morphology and abundant thrombocytes. Blastic infiltration was noted on morphological examination of bone marrow aspirate and biopsy. Leukemic cells exhibited positive reactions to cytochemical stains of periodic acid-Schiff, peroxidase, chloroacetate esterase, and α-naphthyl esterase. The diagnosis of AML-M4 was confirmed by means of immunological phenotyping; the blasts were found to be 80% positive for CD14, 53% for CD13, and 65% for HLA-DR and negative for CD3, CD20, CD10, and TdT. Remission was achieved with a course of mitoxantrone (16 mg/m^2, days 1 and 2) and cytosine arabinoside (400 mg/m^2, days 1–5). He experienced a severe episode of neutropenic fever unresponsive to empirical antibiotic therapy, which would resolve only with the administration of amphotericin B. A second course of chemotherapy consisting of the same agents was given. The patient developed neutropenic fever 4 days after the completion of chemotherapy and was given empirical amikacin and ceftazidime, which proved effective. Concomitantly, recombinant human G-CSF treatment was instituted, 5 μg/kg daily as intravenous infusion over 30 minutes. The white

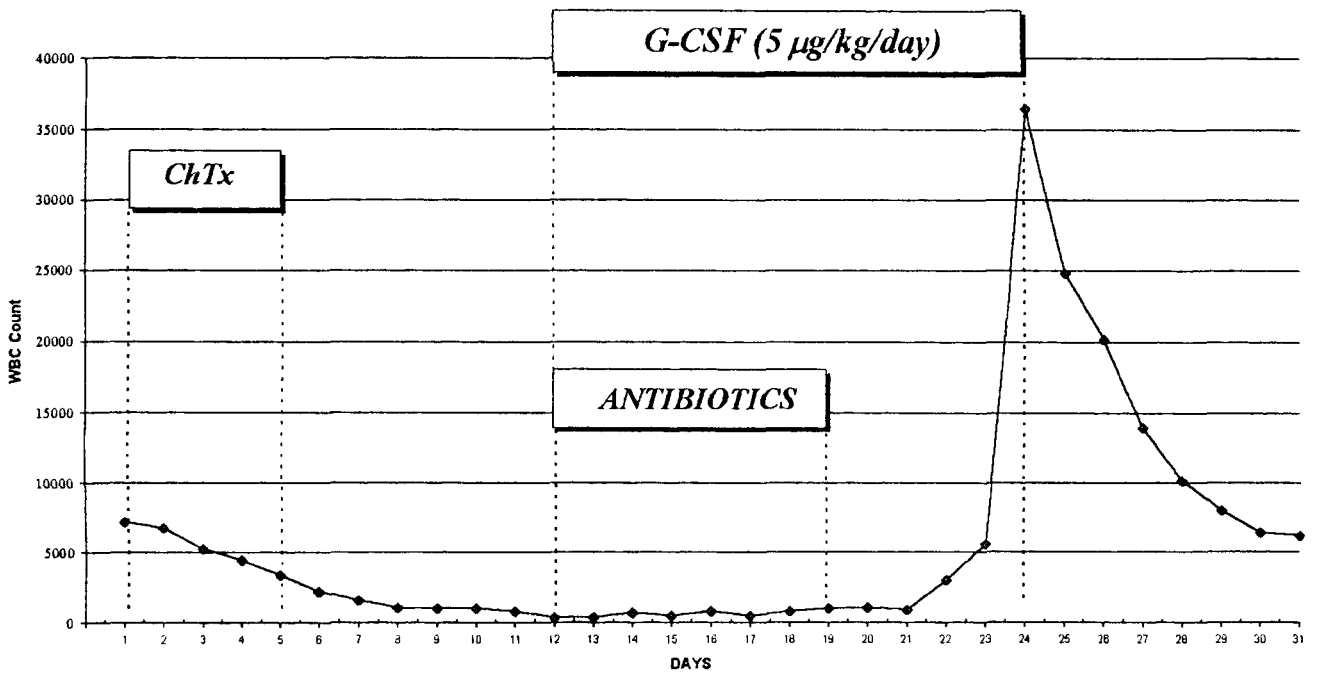

Fig. 1. White blood cell (WBC) count of the patient in relation to chemotherapy (ChTx) and G-CSF administration.

blood cell count increased from 0.4×10^9/L to 1.0×10^9/L in the first 10 days, only to exhibit an accelerated rise afterwards, the count reaching 36.5×10^9/L on the 14th day. G-CSF was therefore discontinued (Fig. 1). The peripheal smear revealed 2% blasts, 3% promyelocytes, 5% metamyelocytes, 14% bands, 58% polymorphonuclear leukocytes, 12% lymphocytes, and 6% normoblasts. Bone marrow aspirate exhibited hypercellularity and marked myeloid hyperplasia (myeloid/erythroid ratio, 8:1), with 1.0% blasts. The white blood cell count declined to 4.6×10^9/L in a period of 8 days. Daily peripheral blood smear examinations revealed the gradual resolution of leukoerythroblastosis. Subsequent bone marrow aspiration was unremarkable except for mild erythroid hyperplasia, with a blast count of 0.5%. On the confirmation of remission, the patient was discharged and was followed as an outpatient on a monthly basis. The patient is well and free of any evidence of relapse after 6 months of follow-up. The exclusion of other possible causes of leukoerythroblastosis such as invasion of the bone marrow with the leukemic clone or infections and the absence of acute hemolysis or sepsis together with resolution of the condition after the discontinuation of treatment have defined G-CSF as the responsible factor for this unexpected finding. After 6 months of follow-up, the patient remains in remission, which can be taken as evidence that leukoerythroblastosis associated with G-CSF administration is a transient and benign condition. We agree with Reykdal et al. [1] that the appearance of blasts may not always indicate relapse, such unexpected effects of G-CSF should always be kept in mind.

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Possible Cytokine Mechanism of Increased Megakaryocytic Proliferation in 5q− Syndrome

To the Editor: We read with interest the excellent article about hematologic features of patients with chromosome 5q deletion by Lewis et al. in the July 1995 issue of the *American Journal of Hematology* [1]. The 5q− syndrome is a clonal hematologic disorder characterized by hypolobulated micromegakaryocytic hyperplasia and a clonal cytogenetic anomaly consisting of an interstitial deletion of the long arm of chromosome 5 (5q−). Increased megakaryocytic proliferation with the characteristic megakaryocyte morphology and the concomitant presence of normal or high platelet counts and leukopenia are from specific features of the 5q− syndrome [1,2].

The proliferation and differentiation of hematopoietic cells is under the control of specific growth factors. Several major hematopoietic growth factors, including interleukin-4 (IL-4), acting on myeloid progenitors are located in the long arm of chromosome 5. On the other hand, the megakaryocytopoietic cytokine IL-6, which seems to be responsible for megakaryocytopoiesis in many cases of reactive thrombocytosis, is located in a different chromosomal location, 7p15 [3,4].

A 32-year-old male patient was admitted to our hospital with the complaints of low-grade fever, malaise, and weight loss. On admission, he had leukopenia (white blood cell count, 1,800/mm^3, with 40% neutrophils in peripheral blood), macrocytic anemia (hemoglobin and mean corpuscular volume, 11.3 g/dl and 92 fl, respectively), and thrombocytosis (platelet count, 996,000/mm^3). Bone marrow examination showed a hypercellular marrow, increased hypolobular micromegakaryocytes, and increased erythroid activity with 10–30% dyserythropoietic precursors. Cytogenetic analysis revealed the 5q deletion breakpoints as (q13:q33). No additional karyotypic abnormality has been found. Serum IL-6 and IL-4 concentrations were 68.3 pg/ml and 0 (undetectable) pg/ml, respectively, in this patient with 5q− syndrome associated with marked thrombocytosis and leukopenia. Normal median serum levels of IL-6 and IL-4, which had been detected in 15 [8 women and 7 men; median age, 26 (range, 24–36)] healthy volunteers with normal platelet counts (range, 191,000–385,000/mm^3), were 5.7 (range, 2.5–21.6) pg/ml and 33.6 (range, 5.1–107.2) pg/ml, respectively, in our enzyme-linked immunosorbent assay laboratory. Therefore, serum IL-6 level was notably increased in this patient with 5q− syndrome while the IL-4 level was found to be significantly decreased.

IL-4 may function directly as a negative regulator of megakaryocytopoiesis and also it inhibits IL-6 synthesis and suppresses IL-6 production in vitro [5,6]. Increased IL-6 concentration in the patient might be due to decreased IL-4 synthesis by reason of the deletion of 5q. IL-6, which has a chromosomal location of 7p15, is a well-known megakaryocyte potentiator [7–9]. Consequently, leukopenia and thrombocytosis in the 5q− patient may be explained by decrease in cytokine interactions by the deletion of the long arm of chromosome 5. Nevertheless, further studies are needed to determine the association between clinical/laboratory hematologic features of patients with chromosome 5q deletion and hematopoietic cytokines.

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Iron Granules in Plasma Cells: A Particular Morphologic Aspect

To the Editor: Iron granules in plasma cells were described in 1938 in a patient with hemochromatosis [1]. They are stained yellow-brown in May-